

* Adrenergic Antagonist *

* Sympatholytics *

α Blockers

• Vaso dilatation

↓
↓ PR

↓
↓ BP

• ↑ reflex
Tachycardia

* Block $\alpha_1 \rightarrow \downarrow PR \rightarrow$
 $\downarrow BP \rightarrow$ reflex Tachy.
 * Block $\alpha_2 \rightarrow \uparrow$ catecholamine
 $\rightarrow \uparrow BP \rightarrow \uparrow CO \rightarrow \uparrow PR \rightarrow$
 reflex bradycardia

β Blockers

* α Blockers *

① Phenoxy-
benzamine

② Phentolamine

③ prazosin

Terazosin
Doxazosin

④ Ergot
alk

⑤ Yohimbine

- α non selective Blocker. ①, ②, ④
- α_1 selective Blocker ③
- α_2 selective Blocker ⑤

خیز نفس عمیق
 اوی به عسلیم الحوار
 کیس به بس حلو
 ولتین صقنی
 به یلا ربنا معال

Adrenergic antagonists

↓
 α - Blockers

↓
 β - Blockers

آنا با عمل که به عسلیم
 بقی عارف احنا ما شیم
 انای و ما تو می منی
 رکز بنا و ص ص ص ص
 ده کو بایه ای که به یلا معال

α - Adrenergic Blockers

- ① phenoxybenzamine
- ② phentolamine
- ③ Prazosin, terazosin, doxazosin
- ④ Ergot Alkaloids
- ⑤ yohimbine

* * * U have to know that those agents mainly affect Blood pressure

* * * Blocking of α receptors \rightarrow induce vasodilation, \rightarrow \downarrow PR \rightarrow \downarrow Blood pressure

* * * this induces reflex tachycardia from lowered BP.

reflex bradycardia و reflex tachycardia \rightarrow این \rightarrow که به یلا معال

① Phenoxybenzamine

- ① Concept of action.
- ② actions.
- ③ Therapeutic uses.
- ④ adverse effects

Phenoxy Benzamine α Blocker

A MoA

- Drug Related to Nitrogen mustards
- α nonselective B.
- $\alpha_1 \rightarrow$ Postsynaptic
- $\alpha_2 \rightarrow$ pre "
- Non Competitive and to overcome this Blocking is b body synthesis new R_s
- Prodrug $\xrightarrow{\text{body}}$ BioTransformation Active form

B Actn

- $\alpha_1 B \rightarrow$ Vasodilatation \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow reflex Tachycardia
- $\alpha_2 B \rightarrow$ \uparrow catecholamines \rightarrow \uparrow CO_P

• Epinephrine reversed why?

- \rightarrow Phenoxy Benzamine Block α effect of epinephrine \rightarrow Vasodilatation \rightarrow \downarrow PR \rightarrow \downarrow BP
- \rightarrow Phenoxy Benzamine not affect β_2 effect of epinephrine \rightarrow Vasodilatation \rightarrow \downarrow PR \rightarrow \downarrow BP

• Nor epinephrine not reversed by only its Actn is decreased. as Nor epinephrine has \uparrow effect on β_2

• Isoproterenol not affected by phenoxy Benzamine as it Pure β Agonist

C Therapeutic uses

① in surgical removal of pheochromocytoma (tumor of Adrenal medulla ???)

② in Raynaud's Disease
السطف، السطف

D Adverse effect

① Postural hypotension (orthostatic -) ???

② Nausea. Vomiting. nasal stiffness.

③ \downarrow male ejaculate (\downarrow Vasoconstrict)

④ \uparrow reflex Tachycardia \rightarrow

C.I in patient \bar{e}

Cranial Perfusion ???

(a) Concept of action :

- * it's a drug related to nitrogen mustards.
- * it's a non-selective blocker \rightarrow bind covalently to (α_1) post synaptic & (α_2) presynaptic receptors.
- * This block is irreversible & non competitive
يعني ملو يربط مع مستقبلات الـ agonist ولا يني أكسر الـ bond الـ receptor. الـ بينه وبينه الـ طبعاً ما يكحل يعني ؟
- * The only mechanism to overcome this block is that the body synthesize new receptors
 \rightarrow this will take a day or more (24 hrs)
- * it's action is slow (delayed) \rightarrow as it's a prodrug \rightarrow requires Biotransformation, to change to its active form.
يعني بيأخذ وقت علشان يستغل وبيأخذ وقت علشان يفت.

(b) Actions :

- * Blocks (α_1) receptors \rightarrow Vasodil. \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow reflex tachycardia.
- * Blocks (α_2) presynap on heart \rightarrow \uparrow catecholamine release on heart causing \uparrow in Cardiac output.
أكي حه هيسأل ويقول حه هو إني من قلت إني القلب ملو هو غير (α_2) nerve حه فإجابتي حه يا حبيبي أنا بأقول حه α_2 presynaptic حه يعني على الـ nerve الـ جاي للقلب حه من الـ receptor الـ على القلب نفسه.
- \rightarrow So \rightarrow reflex tachycardia + \uparrow CO \rightarrow \uparrow BP
- \therefore the effect of phenoxylbenzamine in \downarrow BP is small \therefore its use is discontinued.

⊛ Epinephrine reversal :

→ phenoxybenzamine blocks (α) effect of epinephrine → peripheral vasodilatation, → ↓BP

→ phenoxybenzamine has no effect on (β_2) effect of epinephrine causing dilatation of other vascular beds → ↓BP

∴ phenoxybenzamine causes lowering of BP when given with epinephrine

→ norepinephrine has lower (β) effect

∴ its action isn't reversed but only diminished by phenoxybenzamine.

→ isoproterenol is a pure (β) agonist.

∴ its action isn't affected at all by phenoxybenzamine.

⊙ Therapeutic uses :

⊛ it's used before surgical removal of pheochromocytoma which is a tumour arising from adrenal medulla cells

↑BP due to Adrenaline (α, β agonist) released from adrenal medulla cells during removal of this tissue. α, agonistic action causes ↑BP.

∴ it's used to preclude (prevent) hypertensive crisis (زَجْر) that result from manipulation of this tissue.

⊛ it's used in management (chronic) of these tumours especially if these tissues are diffuse, unremovable (inoperable).

⊛ Sometimes it's used in Raynaud's disease

إنه الدواء يبقى الأطراف ساقة أوى α أدوية phenxybenzamine يعمل peripheral vasodil. من الدم يصل الأطراف. تبقى.

ⓓ Adverse effects :

⊛ it can cause postural hypotension (orthostatic hypotension)

يعني إيه؟

من إيه لما بتيجي تقف فجأة من المفروض إن ال α بتساقط $\uparrow BP$ و $\uparrow PR$ بتساقط من الدم يصل الدماغ

من أنا لو واخني phenxybenzamine من ال α من تساقط من الدم hypotension بتساقط Postural hypoten. من فتحة جامة

⊛ it causes nausea, vomiting, nasal stiffness

⊛ it inhibits male ejaculation, as it prevents vasoconstriction

⊛ induce reflex tachycardia as contraindicated with patients with decreased coronary perfusion

يعني لو واحد عنده مشكلة في ال coronary artery اللي بيغذي عضلة القلب نفسها من المفروض إن أهني القلب عنده هو من واحد غشاء ولا O_2 كويس من ذلك لو مررت به حصل مشاكل في عضلة القلب نفسها

من كده إيه خلاص ال Phenoxybenzamine من هو معلق طويل بس لنين وممكن تلحقه إيه مع نفسك لو فوجئت ال concept بتاعه كويس

من أقالوا نسوق ال

② Phentolamine

ⓐ Concept of actions

ⓑ ind., uses, adv. eff.

Phenoxyl Benzamine (2) Phentolamine α Blocker

A MoA

- non selective α Blocker
- Competitive

B Actn

- $\alpha_1 B \rightarrow$ Vasodilation \rightarrow
 $\downarrow PR \rightarrow \downarrow BP \rightarrow$ reflex
Tachycardia
- $\alpha_2 B \rightarrow \uparrow$ Catecholamines
 $\rightarrow \uparrow CO_P$
- Epinephrine reversal
 $\downarrow BP$
- Nor Epinephrine
 \downarrow its Actn
- not affect Isoproterenol

C Therapeutical uses

- ① only in diagnosis of pheochromocytoma but, phenoxyl Benzamine used in III and surgery why??
as its effect for short time (competitive)

D Adverse effect

- ① Postural hypotension
- ② Nausea, vomiting, nasal stiffness.
- ③ Angina & Arrhythmia due to \uparrow reflex Tachycardia in Patient & coronary Perfusion

(a) Concept of action : phenoxybenz التي ال بالضبط من القوة الوحيدة أد
competitive, reversible

و من حيث في التأثير بين ال action بأنه يتأخر وتأخر

- * it's non selective blocker \rightarrow blocks (α_1) postsynaptic, (α_1) presynaptic
- * this block is reversible, competitive
 \rightarrow so its actn lasts for 4 hrs only.

(b) actions : phenoxybenzamine التي ال التي

- * Blocks (α_1) \rightarrow Vasodil. \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow reflex tachycardia mediated by baroreceptors (baroreceptors).
- * Blocks (α_2) presynaptic on heart \rightarrow \uparrow catecholamine release \rightarrow \uparrow COP
- * epinephrine reversal \rightarrow causes \downarrow BP when taken with Phentolamine.

(c) uses : phenoxybenzamine التي ال

- * used in diagnosis of pheochromocytoma.

only diagnosis \rightarrow التي ال effect بأنه فقط

surgery ال treatment في ال phenoxybenzamine بأنه فقط ال effect بأنه فقط ال الزمن

(d) adverse effects : phenoxybenzamine التي ال التي

- * Postural hypotension (orthostatic hypotension)
- * arrhythmias, anginal pain due to tachycardia in case of patients with decreased coronary perfusion.

phenoxybenzamine التي ال phenolamine ال التي ال

③ Prazosin - Terazosin - Doxazosin α_1 Blocker

A MoA

- Selective α_1 Blocker
- Competitive
- metabolized to inactive sub excreted in urine except Doxazosin \rightarrow faeces.
- Doxazosin have longest Actn

B Actn

• α_1 Blocker \rightarrow vaso. dilatn \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow reflex Tachycardia

N.B it is selective α_1 β

not α_2 \therefore not \uparrow CO, \uparrow

\therefore used III of hypertension

\rightarrow \rightarrow Phentelamine
phenyl Benzamine

C Therapeutical uses

① III of hypertension

N.B \perp First Dose

effect \rightarrow strong

Hypotension \rightarrow

fainting \therefore \therefore

\therefore first dose must

be decreased to $\frac{1}{3}$ -

$\frac{1}{4}$ of N-value.

or Taken at bed

Time.

② instead of surgery

used III of prostatic

hypertrophy - ???

\rightarrow α_1 Blocker \rightarrow

relaxn of smooth

muscles - sphincter of

Bladder \rightarrow urine flow.

D Adverse effect

1. drowsiness - headach

nasal congestn

2. postural hypotension

3. must be \downarrow +

β Blocker - Diuretics

N.B

not affect male

sexual functn

like phenoxy Benzamine

\rightarrow phentelamine

③ Perazosin, Terazosin & Doxazosin

- ① Concept of action
- ② Actions
- ③ Therap. uses
- ④ adverse effects.

① Concept of action :

- * They are Selective & Competitive (α_1) blockers.
- * Metabolism lead to inactive products \rightarrow excreted in urine except doxazosin (in faeces).
- * Doxazosin is longest in actn.

② Actions :

- * They Block (α_1) \rightarrow Vasodil. \rightarrow \downarrow PR \rightarrow \downarrow BP \rightarrow may induce reflex tachycardia
- * But they don't affect (α_2) presynaptic.
 \therefore no \uparrow in catecholamine release at heart
 \therefore no \uparrow in COP
- * So, these drugs are effective in treatment of hypotension
يعني ~~لا~~ في ~~ال~~ phenylephrine, phenylpropanolamine, phenylamine etc
- * they cause minimal changes in COP, renal Blood flow, glomerular filtration rate.

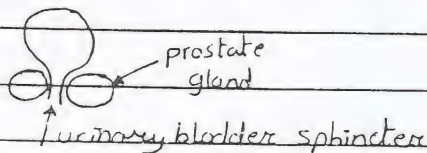
③ Therapeutic uses :

- * treatment of hypertension with no tolerance to their actn.
- * "First dose effect" \rightarrow the first dose of these drugs produce

a very strong (exaggerated) hypotensive effect \rightarrow that causes syncope (fainting) \therefore the first dose must be ~~to~~ decreased to $\frac{1}{3}$ or $\frac{1}{4}$ of normal dose or, Given at bed time.

(*) can be used instead of surgery in patients with benign prostatic hypertrophy

because α_1 block \rightarrow \downarrow smooth muscle contractn, \rightarrow relaxn, of sphincter of bladder \rightarrow improves urine flow



urine flow || sphincter || α_1 block \rightarrow prostate hypertrophy ||
 α_1 block \rightarrow sphincter || relaxn, \rightarrow α_1 blocker \rightarrow prostate ||
 Normal urine flow ||

(D) Adverse effects :

- (*) dizziness, drowsiness, headache, nasal congestn, , lack of energy
- (*) Postural hypotension (orthostatic hypotension) \rightarrow in a lower degree than phenox benzamine, phentamine
- (*) its dose must be \downarrow if used in combinatn, with a diuretic or, with β_1 Blocker.
- (*) Male sexual functn, isn't affected like in phenox benzamine, phentamine

[4] Ergot Alkaloids α Blocker

- 1st Sympatholytic is discovered
- it is considered Partial Agonist α_1 or Antagonist α_1 / α_2 / Serotonin R

[5] Yohimbine α_2 Blocker

→ like reserpine in Structure

→ α_2 Competitive Blocker

→ CNS → ↑ motor Activity → Tremors

→ ↑ Catecholamines Release → ↑ CO₂ → ↑ HR

↑ BP (SBP)

→ used in III of male sexual dysfunction
As cause vasoconstriction

N.B clonidine is α_2 Agonist
Yohimbine is α_2 Antagonist

④ Ergot Alkaloids

- * The first adrenergic receptors antagonist to be discovered.
- * They act as partial agonist or, antagonist at (α) receptors, dopamine receptors, serotonin receptors

إيه يا عم ال partial agonist ده؟ من إيه من بينكم بيقول بوقت ال antagonists
يا عم إيه جاب حيرة ال agonists بوقت؟

→ Partial agonist means produces very little effect, blocks the receptor for in face of more potent drugs

يعني بيقول effect قليل جداً ولو هالك أي drug ال effect قوي تاير
يعني في ال receptor من حيزوف لانه ال partial agonist موجود

⑤ Yohimbine

- * Found in Bark of tree Yohimbe, Rauwolfia roots
- * Its structure is similar to that of reserpine
- * it's an (α_2) competitive antagonist.

- * enters CNS → enhances motor centre activity → produces tremors
- * it ↑ HR (heart rate), ↑ CO → ↑ BP. (especially systolic BP)
- * Used in treatment of male sexual dysfunction, as it ↑ Sympathetic activity by (α_2) presynaptic inhibition,

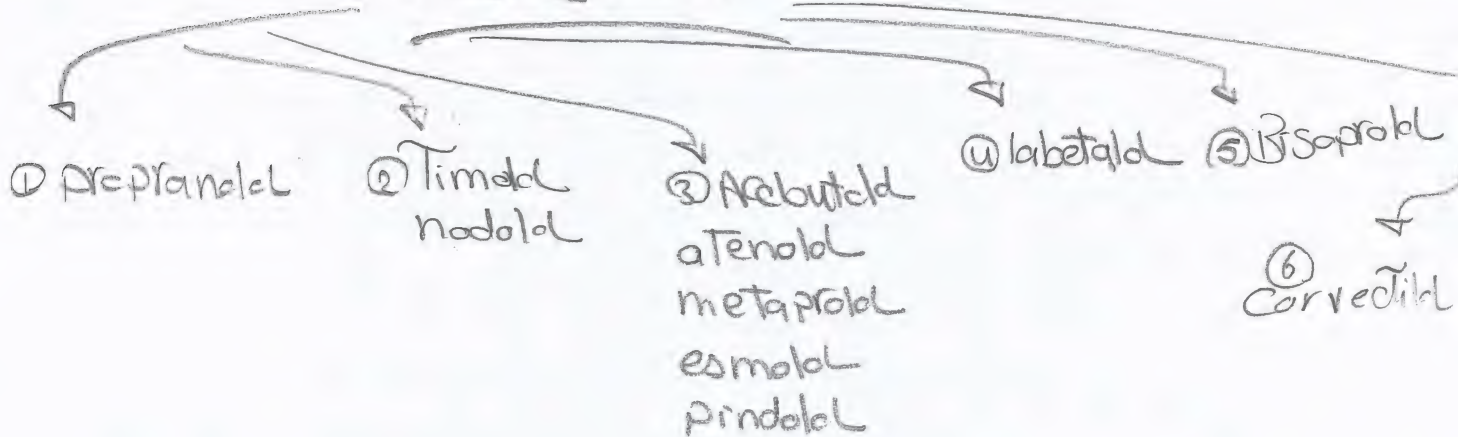
- * these effects are opposite to those of clonidine (α_2 agonist)

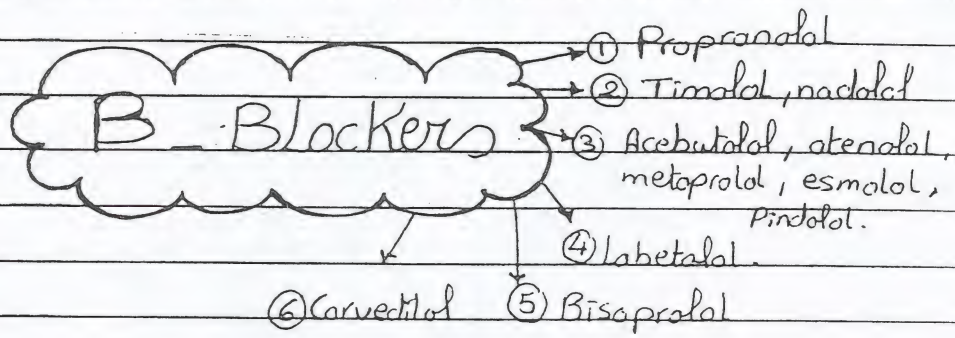
Blockers ال α -blockers ال إيه من بينكم بيقول بوقت؟

* β Blocker *

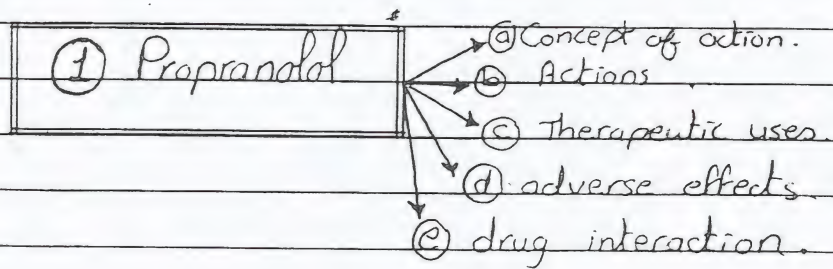
- Non Selective Competitive Blocker
- selective only β_1 (cardio selective)
- ∇ BP but not produce hypotension (postural) like α Blocker
- III Angina - arrhythmia - myocardial infarction
→ bradycardia effect
- III of glaucoma.

* β Blocker *





- * all clinically available β -Blockers are competitive antagonists
- * Non selective act on Both β_1 , β_2
- * Cardioselective " " β_1 only
- * They differ in intrinsic sympathomimetic activity, CNS effects & pharmacokinetics.
- * They Lower BP but don't produce postural hypotension as (α) adrenoreceptors remain functional
- * They are effective in treating angina, cardiac arrhythmias, myocardial infarction, \rightarrow due to its bradycardial effect.
- * Used in glaucoma, prophylaxis of migraine headaches.



و لا بينا نسوقه حجة حجة و خلقناك صبر علينا
هو معلوما في كثير منوية و كذا صحتنا لتيه و كلامه كذا Logic

1) Propranolol β Blocker

A Actn

1) CVS

β Blocker \rightarrow \downarrow CO \rightarrow \downarrow PR
 \rightarrow \downarrow BP -ve Inotropic
 -ve chronotropic
 -ve dromotropic

\downarrow oxygen demand so used
 in III of Angina & Supra-
ventricular arrhythmia
 (due to A.V. - S.A nodes)

β_2 Blocker \rightarrow

Peripheral Vasoconstriction
 • not effect \downarrow SBP \downarrow DBP
 \bar{e} no Postural hypotension

2) Respiratory S

β_2 Blocker \rightarrow Bronchoconstriction
 so CI in COPD, asthma

3) urinary S

β Blocker \rightarrow \uparrow B flow to kidney
 \rightarrow \downarrow Na⁺ retention \rightarrow \downarrow Plasma vol
 \rightarrow \downarrow CO \rightarrow \downarrow BP so
 used \bar{e} Diuretics

4) in glycogen metabolism

β Blocker \rightarrow \downarrow glycogenolysis
 \downarrow glycogen release so
 given \bar{e} cause \bar{e} insulin

B Therapeutic uses

1) III of Hypertension

2) " " migraine

3) \bar{e} Hyperthyroidism
 \rightarrow \uparrow Sympathetic stimulation
 \rightarrow Cardiac erythema.

4) III of glaucoma.

\rightarrow \downarrow IOR as Vasoconstriction
 in Blood vessels feeding
 ciliary body which responsible
 for formation of aq. humour.

NI B not affect on stability of eye

\bar{e} focus for near vision unlike
 other cholinergic drugs.

- used in III of Acute glaucoma
 But chronic glaucoma \rightarrow Pilocarpine

5) Angina - myocardial infarction

N. B - Isoproterenol $< \beta_1$ Agonist
 so Blocked by Propranolol

- Epinephrine $\left\{ \begin{array}{l} \beta_1 \\ \beta_2 \end{array} \right\}$ blocked by Prop.
 α_1 \rightarrow not affected

- nor Epinephrine α only so not affected \bar{e} Propranolol.

C Adverse effect

1) Broncho Constriction
 CI in asthma, COPD

\rightarrow air entering lung \rightarrow
 Asphyxia \rightarrow Death

2) Arrhythmia -
 If quickly stopped \downarrow III
 so stopped must be
 gradually

3) Sexual impairment \rightarrow α

4) Disturbance in
 metabolism

\rightarrow insulin dependent
 Patient + β Blocker

\downarrow hypoglycemia
 \downarrow hyperglycemia

NI B Patient \bar{e}

Diabetic, asthma must
 not be III \bar{e} β Blocker

\downarrow
 Cardioselective β_1
 Blocker

D InterActn

1) Propranolol +
 \downarrow its metabolism

\downarrow
 \uparrow effect

e.g. Cimetidine (H_2R
 in stomach)
 Block

• furosemide
 (Diuretics)

• Chlorpromazine
 (antipsychotic)

2) Propranolol +
 \uparrow its metabolism

\downarrow
 \downarrow effect

• Barbiturates

• rifampin (anti TB)

• phenytoin
 (antiepileptic)

@ Actions :

i) Cardiovascular :

* \rightarrow it \downarrow COP by -ve inotropic, -ve chronotropic, -ve dromotropic effects. \rightarrow this bradycardial effect limits the dose of drug to be taken

* \rightarrow Cardiac work, oxygen demands are \downarrow by β_1 block
 \therefore useful in angina treatment.

* \rightarrow useful in case of supraventricular arrhythmias which is the arrhythmia of S.A. node, A.V. node

الاضطرابات التي تنشأ في البطينات ~~supraventricular~~ \rightarrow ventricles

But \rightarrow not useful in case of ventricular arrhythmias

* Peripheral Vasoconstriction \rightarrow @ By blocking β_2 which causes vasodilatation,
 \rightarrow @ the decrease in BP \rightarrow due to \downarrow COP induces reflex vasoconstriction.

* The net effect is gradual \downarrow in systolic, diastolic BP.
But with no postural hypotension (α_1 isn't affected)

ii) Respiratory :

* \rightarrow Blocking (β_2) may cause Bronchiolar smooth Ms contraction, this can cause a respiratory crisis in patients chronic obstructive pulmonary disease or, Asthma

\therefore β_1 Blockers are contraindicated in patients with asthma.

iii) Urinary :

* the \downarrow Blood flow causes \downarrow in renal perfusion which causes \uparrow in Na^+ retention

* this Na^+ retention \uparrow osmolarity of Blood \rightarrow absorbing H_2O from nephron tubules back to blood $\rightarrow \uparrow$ plasma volume.

* when plasma volume $\uparrow \rightarrow$ The COP slightly $\uparrow \rightarrow \uparrow$ BP

so

β -Blockers are usually used with diuretics to prevent Na^+ retention $\rightarrow \downarrow$ plasma vol \rightarrow COP $\rightarrow \downarrow$ BP

iv) Glycogen metabolism disturbance :

* β_2 Block $\rightarrow \downarrow$ glycogenolysis, \downarrow glucagon release

so insulin dependent patients taking propranolol should monitor blood glucose very carefully. Because they may cause very strong hypoglycemia after insulin injection.

v) Blocks action of isoproterenol :

* isoproterenol $\rightarrow \beta_1 \rightarrow \uparrow$ COP $\rightarrow \uparrow$ Systolic BP
(has CH_3 group) $\rightarrow \beta_2 \rightarrow$ Vasodil $\rightarrow \downarrow$ PR $\rightarrow \downarrow$ diastolic, mean BP
these effects are blocked by propranolol.

* epinephrine $\rightarrow \beta_1 \rightarrow \uparrow$ COP $\rightarrow \uparrow$ systolic BP
works on both $\beta_2 \rightarrow$ Vasodil $\rightarrow \downarrow$ PR $\rightarrow \downarrow$ diastolic, mean BP
(α, β) $\rightarrow \alpha \rightarrow$ Vasocons $\rightarrow \uparrow$ PR $\rightarrow \uparrow$ diastolic, mean BP

Blocked by
Propranolol

this effect isn't stopped by β -Blockers

* norepinephrine \rightarrow only α effect \rightarrow so not affected at all by propranolol.

(b) Therapeutic uses :

i) Hypertension :

→ it lowers BP by \downarrow CO_P

ii) Glaucoma :

→ it \downarrow intraocular pressure by β_2 Block causing vasoconstriction of blood vessels feeding ciliary body which is responsible for aqueous humor formation.

→ it has the advantage that it doesn't affect the ability of eye to focus for near vision, doesn't change pupil size as cholinergic drugs.

→ it's used only in chronic glaucoma treatment. But in acute attacks of glaucoma → pilocarpine is the drug of choice.

iii) Migraine :

→ it blocks (β_2) vasodilatation in Brain vasculature.

iv) Hyperthyroidism :

→ hyperthyroidism causes \uparrow sympathetic stimulation that may cause serious cardiac arrhythmias.
عقبه ليل: عيبه. hyperthyroidism عيبه ليل

→ this effect is \downarrow by propranolol.

v) Angina pectoris :

- it ↓ HR, CO, P → & ↓ Cardiac work
- ∴ ↓ oxygen requirement of heart muscle
- ∴ reduces chest pain on exertion (work)
- ∴ Propranolol is useful in chronic management of stable angina (not for acute angina attacks).

vi) Myocardial infarction :

- Propranolol has protective effect on myocardium.
- it's used prophylactically to prevent a second attack in case of patient that suffered from one attack.
already
- Propranolol administration immediately after a myocardial infarction may reduce size, hastens recovery.
- it reduces the incidence of Sudden arrhythmic death after myocardial infarction.

© Adverse effects :

- Bronchoconstriction
- Arrhythmia
- Sexual Impairment
- Disturbances in metabolism.

1] Bronchoconstriction :

أحنا عارفين انه بيغل bronchoconstriction بسبب انه بيقلل ال β_2 مطب لو المريض ده عنده asthma - يعني ال lungs عنده أصلاً متقفولة ← يبقى لما اديله الدواء ده ← نفس كيعرف يتنفس وهيموت.

* Propranolol has a serious and potentially lethal side effect when administered to an asthmatic. why?!

- because an immediate contraction of the bronchial smooth muscles prevents air from entering the lungs

∴ Deaths by asphyxiation (عنت القدرة على التنفس) have been reported for asthmatics who were administered the drug.

∴ Propranolol must never be used in treating any individual with obstructive pulmonary disease.
وعرفنا ليه ∴ ∴ ∴

2] Arrhythmia :

Treatment with the β -blockers must never be stopped quickly why?!

- because of the risk of precipitating cardiac arrhythmia which may be severe. As long term treatment with an antagonist leads to up regulation of the β -receptors.

يعني اي واحد بياخد ال propranolol لما يتنفس يوقف العلاج مرة واحدة عنده خطر من arrhythmia ، مطب ليه ؟!

علشان ال antagonist ده لان قافل ال receptors ، فلما آجي
أوقف مرة واحدة ← يبقى كل ال β_2 receptors (اللى على القلب)
اللى كانوا معقولين دول هيفتحوا مرة واحدة و يشغلوا
جامد ← يعطوا arrhythmia

∴ The β -blockers must be stopped gradually for
1 week.

- On Suspension of therapy → the increased receptors
can worsen angina or hypertension
لما اوقف العلاج مرة واحدة

[3]

Sexual Impairment:

دى غريبة شوية ← علشان ال male sex organs بيشتغل
على α receptors ، فالمفروض ان ال β blockers ما يتيسر
تأثير عليها ← لكن وجبنا برده انك بيحل impaired sexual activity
فربعض المرفه اللى خدوا الدواء ده ← بين السبب من معروف

* Since sexual function in the male occurs through
 α -adrenergic activation → β -blockers may not affect
normal ejaculation nor the internal bladder sphincter
function.

4 Disturbances in metabolism:

هو بيقفل ال β_2 receptors ال بتؤد ال glycogenolysis
 وال glucagon secretion \leftarrow \uparrow glucose \leftarrow hyperglycemia
 يبقى لما اقل ال receptors \leftarrow \downarrow glycogenolysis و
 hypoglycemia \leftarrow \downarrow glucose \leftarrow \downarrow glucagon secretion
 . سلو كده ! طب فين المشطلة بقى !

الدمشطلة لو حده مريض عنده diabetes بين من النوع insulin dependent
 دفين بياخد insulin عكسها يقل ال glucose ال في الدم و الدواء
 اصلاً عادله hypoglycemia \leftarrow يبقى ال glucose عنده هيقفل
 بطريقة حادة أوى وخطر .

* β -blockers leads to \downarrow glycogenolysis and \downarrow glucagon secretion \rightarrow ∞ Fasting hypoglycemia may occur.

يبقى لو عاين اقل الضغط لو احد عنده asthma او insulin dependent diabetes

يبقى من هديف استئتم nonselective β -blockers لكن استئتم حاجة
 selective بتشتغل بين على ال β_1

∞ Cardioselective β -blockers are preferred in treating insulin dependant asthmatics .

دلو في كوستون آخر حدة في ال Propranolol و في ال
 Drug Interactions .

(d) Drug Interactions :

طبیعی ان ای ادویه تقلل تکسیر او ال metabolism بتاج
 ال propranolol ← هتزوڈ ال effect بتای
 وای ادویه بتزوڈ ال metabolism بتای ← بتکسر اکثر
 ← هتتل ال effect.

* Drugs that interfere with the metabolism of propranolol as :-
 - cimetidine (H₂ blocker for peptic ulcer)
 - furosemide (diuretic)
 - chlorpromazine (antipsychotic)
 → potentiate its antihypertensive effect.

• while, drugs that stimulate its metabolism, such as :-
 - barbiturates
 - phenytoin (antiepileptic)
 - rifampin (anti TB)
 → ↓ its effect.

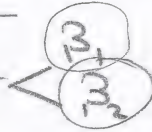
(2) Timolol and Nadolol

* معلومة لیک لتسهل الفظ
 کل ال β -blockers آخر اسمهم (-olol)
 مانند ال Labetalol وال carvedilol ← آخرهم (-al) بس.

عیب تقالوا بتقول طمستین که علی الدوائیین دول ← متی هتطوّل
 Propranolol ۰۰۰۰

✓ [2] Timolol - Nadolol β Blocker

• non selective β Blocker



• more potent than Propranolol

• Nadolol \rightarrow v. long duration of action

• Timolol \rightarrow \downarrow production of aqueous humour in eye
So used in open angle glaucoma
and hypertension

* Timolol & Nadolol are non selective β -blockers (i.e. block β_1 & β_2 adrenoceptors)

بين زي ال Propranolol ، بين الفتر

they are more potent than Propranolol.

* Nadolol \rightarrow has a very long duration of action

* Timolol \rightarrow \downarrow the production of aqueous humor in the eye & is used topically in the ttt of chronic open-angle glaucoma
- also used occasionally for systemic treatment of hypertension.

بين كره \leftarrow خلطينا الاتيين دول \leftarrow شايعين السريعة . . .

③ Acebutolol, Atenolol, metoprolol and Esmolol

\downarrow
Selective β_1 antagonists

دول selective بين يشتغلوا على نوع واحد من ال receptors ال
هو β_1 (بتاع القلب) \leftarrow يبقى ممكن استخدمهم علشان اقل الخطر
وانت تقاديت ال unwanted bronchoconstrictor effect ال كان
بيديه ال propranolol في ال asthmatic patients بسبب تأثيره
على ال β_2 receptors

β_1 selective β [3] Atenolol - ²⁾Esmolol - metoprolol - ³⁾Acebutolol - ⁴⁾pindolol
 • β_1 selective β . They are Antagonist for β_1 but does 50-100 times less than
 These required for β_2 R.
 * Acebutolol, pindolol have intrinsic Agonist Activity (Partial Agonist)

A Actn

- \downarrow COP - \downarrow HR
- $\rightarrow \downarrow$ BPS = used in III of Angina & Hypertension
- Esmolol have short life time as metabolize \bar{e} ester linkage
- \rightarrow I-V
- \rightarrow β_2 x so no Bronchoconstrictn

β uses

- Cardioselective β Blocker is useful for hypertensive patient \bar{e} COPD or insulin dependant patient as it avoid β_2 effect

A Actn

- Antagonist with Partial Agonist Activity
- have intrinsic sympathetic activity (ISA)
- \bar{e} have lability of weakly stimulated β_1, β_2 R
- \downarrow lipid, Carbohydrate metabolism.

β Therapeutic Uses

- 1) III of hypertension \bar{e} moderate Tachycardia why???
- 2) III of diabetic

* طبع هو ازای β_1 selective یعنی استمغه همسك في ال β_1 بي؟!

ده بسبب اننا بنحتاج منه dose قليلة علشان يدي تأثير على ال β_1 receptors 50 يعني ايه برده؟!
يعني مثلاً لو ادبت dose عبارة عن 50mg ← دي كافيت
انها تدي تأثير وبقسك في ال β_1 receptors بيبي سس هتسك
في ال β_2 receptors ← يعني selective
لكن لو زودت ال dose ← مثلاً 150mg ← كده همسك في الاشين
 β_1 & β_2 وكده سقاش selective خلاص 500
نكتب الكلف ده يعني 5000

* Cardioselective β_1 blockers, such as Acebutolol, Atenolol, and Metoprolol → antagonize β_1 receptors at doses 50 → 100 times less than those required to block β_2 receptors.

∞ This Cardioselectivity is thus most pronounced at low doses and is lost at high drug doses.

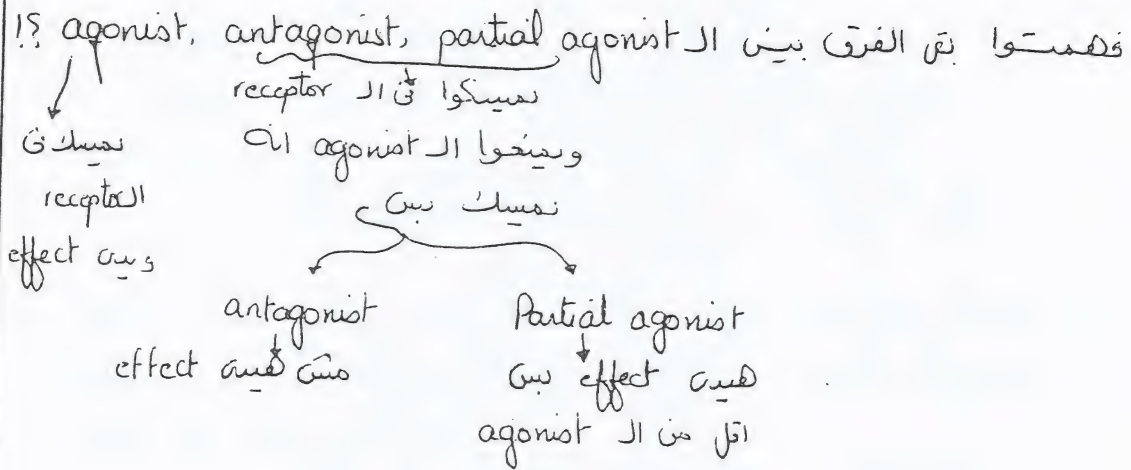
Dr. B's Acebutolol has some intrinsic agonist activity

• يعني ايه؟!.

- الطبيعي في ال antagonists انهم بييسكوا في ال receptor
ويتقلوه فيمنعوا ال agonist من انه يمسك فيه ← يعني يعملوا
blocking ← ده الى احنا عارفينه ← طوكه؟!.

امثال ايه ماله ال Acebutolol ده؟!
- ده يعني يمسك برده في ال receptor ويمنع ال agonist
من انه يمسك فيه ← بيبي سس بيحل complete blocking

لكن بين effect بسيط زي ال agonist ← بنسبه
Partial agonist.



يارب تكون و هلت خلوه

طب هتشفو فيهم حاجتيه دلوقت

1. actions

2. Therapeutic uses.

④ Actions :

احا هنتكلم عن ال atenolol, metoprolol, esmolol
ال Acebutolol نسبيوه ← هنتكلم عليه بعد شويه ...
يقع احنا الى هنتكلم عنهم دلوقت هتكون antagonists عاينين ...

* These drugs ↓ blood pressure in hypertension & ↑ exercise tolerance in angina

* Esmolol has a very short lifetime due to metabolism of an ester linkage

بيتكسر بسرعة ← فينطرح من الجسم بسرعة

as it's only given IV if required during surgery or diagnostic procedures.

* In contrast to Propranolol (Non selective) → these Cardio specific blockers have relatively little effects on pulmonary function, peripheral resistance (no α effect), and Carbohydrate metabolism (no effect on β_2 receptors)

However, asthmatics treated with these agents must be carefully monitored to make certain that respiratory activity is not compromised.

علامة احنا قلنا ان ال dose لو كترت ← من في (في) selective
والمسك في ال β_2 ← ال ممكن تفل bronchoconstriction
فلان انا ال dose حلو اوى بالذات لو عنده asthma

② Therapeutic Uses:

مادام هو selective ← يبقى استخدمه لتقليل الضغط عند مريض
عنده مشكلة من ال Pulmonary fr. او عنده diabetes
ويلاقي insulin (لان احنا قلنا في ال propranolol ← انه ممكن
يقل Fasting hypoglycemia) لكن هنا فيه التأثير على القلب
بس ← فالوقت نوه حاجة تاني

* The Cardioselective β -blockers are useful in hypertensive patients with impaired pulmonary function.
also useful in diabetic hypertensive patients who are receiving insulin or oral hypoglycemic agents.

* Since these drugs have less effect on peripheral vascular receptors \rightarrow Coldness of extremities (a common side effect of β -blocker therapy) is less frequent.

④ Pindolol and Acebutolol

↓
antagonists with Partial agonist activity

احنا بكتيبا خدوس العقبة دي في اد acebutolol ← انا معرفش هو
محبوب هناك معلوم ليه ← بس هو هذا اوضح .

④ Actions :

⊕ Cardiovascular:

* Acebutolol and Pindolol are not pure blockers \rightarrow instead they have the ability to weakly stimulate both β_1 & β_2 receptors & are said to have intrinsic sympathetic activity (ISA)

• sympathetic effect \rightarrow زيادة في سرعة القلب

* These partial agonists stimulates the β -receptors to which they are bound \rightarrow yet they inhibit stimulation by the more potent catecholamines, epinephrine & norepinephrine (agonists)

يعني هذا effect بين اسهل بكثير من ال effect بناع
ال agonists واكثر ملجا من ال antagonists

∴ Produces a much diminished effect on cardiac rate & cardiac output, compared to β -blockers without ISA.

② Decreased Metabolic effects:

* Blockers with ISA \rightarrow ↓ disturbances of lipid & Carbohydrate metabolism seen with other β -blockers.

② Therapeutic Uses:

* β -blockers with ISA are effective in hypertension, with moderate bradycardia \rightarrow since a further ↓ in heart rate is less pronounced with these drugs

وهو سبب ال Partial agonist effect \leftarrow يعني هذا يقلل ال receptors
من ال normal agonists \leftarrow وبالتالي يقلل الضغط لكن من
نفس الوقت من قاذله \leftarrow completely \leftarrow يعني effect خفيف
فمنش هذا bradycardia جامد
يعني لو مثلاً ال antagonist العادي يقلل ال heart rate من
70 \leftarrow 20 \leftarrow مثلاً يعني .

لكن ال partial agonist ده يقلل من 70 \leftarrow 40
يعني هو عمل بده bradycardia بين اقل من ال complete blockers
ماشي

✓ 4) labetalol ($\alpha_1\beta$ Blocker)

ACTION

- α Blocker \rightarrow Vasodilation

$\rightarrow \downarrow PR \rightarrow \downarrow BP$

- β Blocker \rightarrow Vasoconstriction

$\rightarrow \uparrow PR \rightarrow \downarrow BP$

net

\therefore Cause peripheral vasodilation
unlike other β Blocker, produce
peripheral vasoconstriction

\rightarrow doesn't alter serum
lipid or blood glucose level

uses

① $\text{III} = \downarrow$ Hypertension in
Patient $\rightarrow \uparrow$ peripheral
vascular resistant
(black hypertensive
patient)

② alternative of
hydralazine (III
hypertensive
pregnancy)

adverse effect

* orthostatic hypotension

- * Carbohydrate metabolism is less affected with acebutolol & pindolol, than it is with Propranolol
∴ they are valuable in the treatment of diabetes.

⑤ Labetalol



يعين في نفس الوقت

Reversible β -blocker with concurrent α -blocking actions

يعين بيقفل الـ α, β ← طب لما يقفل الـ α ← تصحبل ايه؟
يعمل vasodilatation و هيقل الـ blood pressure عن طريق
انه هيقل الـ peripheral resistance

لكن انا كانوا بيقلوا الـ β بس ← كانوا برده بيقلوا الـ B.P.
بس كانوا بيعالوا vasoconstrict و بيؤدوا الـ peripheral resistance

- * Labetalol cause peripheral vasodilation → ∴ ↓ blood pressure

∴ Contrasts with other β -blockers that produce peripheral vasoconstriction

∴ It's useful in treating hypertensive patients for whom increased peripheral vascular resistance is undesirable

- * Labetalol doesn't alter serum lipid or blood glucose levels.

① Therapeutic Use in hypertension:

* Labetalol is useful for treating the elderly or black hypertensive patients
 يعني مراحل متأخرة أو severe من الـ hypertension ← لهم فيها ان
 ↓

increased peripheral vascular resistance is undesirable

[In general, black hypertensive patients are not well controlled by β -blockers]

فاستخدمهم الـ α -blockers زي الـ labetalol.

* Labetalol may be employed as an alternative to hydralazine in the treatment of pregnancy induced hypertension.

يعني عايزه يقلل لي الضغط من غير مايجل vasoconstrict.

② Adverse effects:

Orthostatic hypotension & dizziness are associated with α -blockade

يعني ايه Orthostatic hypotension ؟

ده الحاحو لما بييج يقف مرة واحدة يدوخ ؟
 علشان الـ α -blockers دول عاملين hypotension ← وده يعني
 الـ peripheral vasodilation ← فالإنسان ده لما يكون قاعد
 أو نيم ← الدم كله هينزل لآحت وما فيش resistance لتزول الدم
 ده ← فلما بييج يقف مرة واحدة ← مفروض الطبيعي ان الـ α -receptors

✓ [5] Bisoprolol β_1 Blocker

- selective β_1 β & also ISA
- Bisoprolol \rightarrow + ACEC (~~Acetylcholine~~ -esterase) inhibitor
 \rightarrow + Diuretics
- III of chronic heart failure
- III of hypertension.

\rightarrow Cause bradycardia - hypertension - fatigue

\rightarrow orally bioavailability 90%

\rightarrow eliminated by renal excretion (58%)

\rightarrow metabolized in liver

\rightarrow plasma half life 11 \rightarrow 17 hrs

مقارنة Nadolol & Bisoprolol in half life
 \rightarrow

تزداد B.P فيروج peripheral vessels الى حائل في vasoconstriction
 فيمنع انه ينزل ← كه التنظيم وال brain ومله في كويين .
 لكن لما اقل ال α receptors ← ال brain من ومله في لقاية
 ← يدوخ وحين انه هيغي عليه ← اسمه Orthostatic hypotension

⑥ Bisoprolol

↓
 highly selective β_1 receptor antagonist that has no ISA or membrane stabilizing activity.

- * Bisoprolol is well tolerated and side effects include : dizziness , bradycardia , hypotension & fatigue.
- * Bisoprolol can be considered a standard treatment option when selecting a β - blocker for use in combination with ACE (Acetylcholine esterase) inhibitors & diuretics in patients with moderate to severe chronic heart failure & in treating hypertension.
- * Bisoprolol is well absorbed after oral administration with bioavailability of $\approx 90\%$
 - It is eliminated by renal excretion (50%) & liver metabolism to pharmacologically inactive metabolites (50%)
 - It has plasma half life of 11 → 17 hrs.

long duration of action ← بين المول واحد قو ؟! فاكين ؟!
 Nadolol →

bravo علي

✓ [6] Carvedilol $\beta_1, \beta_2, \alpha_1$ Receptor

- like labetalol ^{وینبرگول} \rightarrow Antioxidant & anti-proliferating effect
 \rightarrow membrane stabilizing activity ???

Depolarization is

- Lack ISA

- α_1 Blocker \rightarrow vasodilator & antioxidant & anti-proliferating so used in III
at Congestive Heart failure (CHF) ???
- is rapidly absorbed in oral \rightarrow plasma conc. 1-2 hrs and as it is lipophilic
distributed in \rightarrow interstitial fluid (half life 7-10 hr)
- first pass effect

⑦ Carvedilol



third generation β receptor antagonist that has a unique pharmacological profile.



It blocks β_1 , β_2 & α_1 receptors (similar to Labetalol)

سبب زیاده علیه کمانا عیو

a- antioxidant & antiproliferative effects.

b- membrane stabilizing activity

زیاد ← anaesthesia ← Na^+ stabilization ← cell ← depolarization ← anaesthesia

c- It lacks intrinsic sympathomimetic activity.

* Uses & Action:

- Carvedilol produces vasodilation (due to α_1 blocking).
- It is thought that the additional properties (antioxidant and antiproliferative effects) → contribute to the beneficial effects seen in treating Congestive heart Failure. (CHF)

CHF Carvedilol ده کمانا بیالوا ال

بیشتر ال

طب استعصاف

کمانا فی ال CHF ← proliferation ← و ال Carvedilol عیو antiproliferative effect.

Cardiomegaly عیو حجم القلب بیکر

- * Carvedilol is rapidly absorbed following oral administration (peak plasma conc. occur in 1→2 hrs)
- * It is highly lipophilic → ∴ rapidly distributed in extravascular tissues (interstitial fluid)
- * It is 95% protein bound & extensively metabolized in liver.
- * It's half life from 7 → 10 hrs.

يعني هو يمتصه. absorption سريعة ← ييزيد في plasma خلال
ساعة او ساعتين ← ويذهب من ال plasma لل interstitial fluids
∵ highly lipophilic ← لكن في كمية كبيرة منه 95% يتصل
في ال protein وبالتالي مش يدخل الخلية وبتتكرر في ال liver
والى بيخزل الخلية 5% ايسر.

غير انه ممكن يحصل له كان first pass effect لان ال oral
بين نه مش بيخزل لكه ∴ ∴ ∴

Stereoselective 1st pass metabolism results in more
rapid clearance of S(-) Carvedilol than R(+) Carvedilol.

↓
هيتكرر اكثر.

كه خلينا ال α Blockers ووراها ال β -Blockers وشنا
الادوية اللى عليهم ∴ ∴ ∴ دلوقتى هتشرح نوع جديد ← هو α -antagonist
بين عريقة مختلفة ← يك اقلب عليه تسوفه
↪

Drugs affecting Neurotransmitter Release or uptake

افكر معايا كده في ال agonists ← كنا قلنا انه من طه لازم يستغل على ال receptor نفسه ← لكن في ادوية زي ال amphetamine & tyramine دول بيؤدوا ال effect بده بس عن طريق ايزوؤوا ال release بتاع ال Neurotransmitter من ال storage vesicles. ← صبح ؟!

طبيب : هكنا نفس الفكرة ← انا هغير ال effect بس من غير ما جرح حبة ال receptor ← انا هسكن على ال neuron ← يا إما اقل ال release بتاع ال neurotransmitter ← يا إما اقل ال uptake بتاع ال neurotrans. من ال storage vesicles ← effect ↓
او هقتل ال reuptake في ال nerve ← effect ↑ زي ال cocaine
* هتاخذ فيه ٣ ادوية :

- 1- Reserpine
- 2- Guanethidine
- 3- Cocaine

ياك نبتدي فيهم وهتلقوهم سهلين جداً وكلامهم بسيط ٥٥٥

كن مطمئناً جداً ٥٥٥٥
ولا تفكر في الأمر كثيراً ٥٥٥٥
بل دح الأمر لمن بيده الأمر ٥٥٥٥

Pray 4 us a lot ٥٥٥٥٥٥٥٥٥٥

Drug affects neurotransmitter release or uptake

① Reserpine

② Ganithidine

③ Cocaine

① Reserpine

→ plant alkaloid

Actn → block Mg^{+2} / ATP dependent Transport of biogenic amines (NE, Dopamine - Serotonin) from ^{Cyto}Plasm into Storage vesicles in Adrenergic nerve of all tissues -

→ Go NE in cytoplasm - so it is degraded by MAO so
↓ level of NE → ↓ sympathetic function

→ Hypertensive patient → reserpine
* gradually ↓ in BP
* ↓ slowing in HR.

→ slow onset of Actn → long duration

↓
Go if stopped & Actn is persist for many days

Reserpine

↓

block storage

↓

NE still in cytoplasm

↓

MAO degradation

↓

↓ NE level

↓

↓ sympathetic function

1. Reserpine

* Reserpine, a plant alkaloid \rightarrow blocks the Mg^{+2}/ATP dependant transport of biogenic amines (norepinephrine, dopamine & serotonin) from the cytoplasm into the storage vesicles in the adrenergic nerves of all body tissues.

يعتبر احنا عارفين ان ال norepinephrine بيتخزن في ال nerve ويتخزن في ال storage vesicles. وقت ما يحصل excitation وده release \leftarrow تمام. ١٥

طب ال reserpine ده هيقف تخزين ال norepinephrine \leftarrow فدهم في ال cytoplasm \leftarrow طب ايه المسطرة ١٥ المسطرة ان ال cytoplasm فيه MAO \leftarrow اللى بتكسر ال free norepinephrine \leftarrow تمام. ١٥

Monoamine oxidase (MAO) can degrade the norepinephrine in the cytoplasm \rightarrow this causes an ultimate depletion (i.e. decrease) of norepinephrine levels in the adrenergic neuron.

So Sympathetic function, in general, is impaired due to \downarrow release of Norepinephrine.

* Hypertensive patients taking the drug shows a gradual \downarrow in blood pressure & slowing of the cardiac rate.
The drug has a slow onset of action but long duration of action.

MAO \leftarrow ال storage \leftarrow ال وقت \leftarrow ال slow onset *

2) Guanethidine

Actn → Inhibits response of Adrenergic nerve to stimulation or any indirect Acting sympathomimetics amin.

How???

- ① block release of E. from storage vesicles. →
↓ NE → ↓ BP → ↓ HR → ↑ Parasympathomimetic in GIT
- ② Displace NE in storage vesicles → ↑ BP

S-E → Orthostatic Hypotension - interfere w male sexual function

w in patient w pheochromocytoma

supersensitivity to NE due to ↓ release ???

↑
Cold preparatn is phenylpropanolamine

يبتدى يكسر ال Free N.E. غير انه لسة هياخد وقت حد ما خلص
الى كان متخزن املا

وال long duration of action ← لان هنا مش هفعل receptor سوية

واسيب ← لا انا ↓ من الاملا ← يعني املا مش هيكون في
Norepinephrine في ال storage vesicles علشان يطرح
وعلى كده

When one stops taking the drug → the action persists for many days.

لو ما يبيع new norepinephrine بل الى كسره ال HAO

2 Guanethidine

* It inhibits the response of the adrenergic nerve to stimulation or to indirectly acting sympathomimetic amines

↓ how?!

1- by blocking the release of stored epinephrine from the storage vesicles

→ this results in gradual ↓ of blood pressure in hypertensives & a ↓ in cardiac rate.

also there is remarkable ↑ in parasympathetic tone of the GIT...

2 - Guanethidine also displaces norepinephrine from storage vesicles (thus producing transient ↑ in blood pressure)

يعني يزيل نوريبيفرين من storage vesicles ويطلق الـ Norepinephrine
 به ← وبالتالي يحصل زيادة في الـ BP بين حاجة لفترة يعني
 وبعدين هيقول .

طبعا الـ NE اللى بيطلق به ده هيتكسر

∴ this leads to gradual ↓ of NE in nerve endings except those in the CVS.

* Guanethidine is now rarely used in the treatment of hypertension → as it commonly causes orthostatic hypotension & interferes with male sexual function.

النتيجة اللى جاية دي الـ orthostatic hypotension ∴ ∴

* Supersensitivity to NE due to depletion of amine can result in hypertensive crisis in patients with pheochromocytoma

∴ tumor في الـ adrenal medulla

Guanethidine يعني هيقول بقتيل الـ NE من الـ

فيعمل كمان الـ receptors ← فالـ receptors هتبقى

← supersensitive يعني اقل كمية من الـ NE تسوفها

هتكون effect جاية ← ممكن تقى hypertensive crisis

* due to supersensitivity → patients taking cold preparations containing phenylpropanolamine also have exaggerated hypertensive response.

* ودي برده ما اتقال ∴ ∴

∴ Symp. effect جاية اوى

[3] Cocaine

Actn → block $\text{Na}^+/\text{K}^+\text{ATPase}$ which required for reuptake of NE by Adrenergic neuron

↓
NE is Accumulate in synaptic cleft

↓
↑ sympathetic Activity

So ↓ Dose of Catecholamines is individual taken Cocaine
This magnified effect and ↑ duration of Actn

3 Cocaine

أحنا عارفين ان ال NE بعد ما يطرح في ال synaptic cleft في حبة

منه بيحطه reuptake في ال nerve ويتكسر بـ HAO
 ال Cocaine بيوقف ال uptake ده ← وبالتالي
 ال NE هينقى في ال synaptic cleft ← sympathetic activity ↑

* Cocaine is unique among local anesthetics in having the ability to block the Na^+/K^+ ATPase (required for cellular uptake of NE) across the cell membrane of the adrenergic neuron

→ ∴ NE accumulates in the synaptic cleft → resulting in enhancement of sympathetic activity & potentiation of the actions of epinephrine & NE.

∴ Small doses of the catecholamines produce greatly magnified effects in an individual taking cocaine as compared to one who is not.

* In addition, the duration of action of epinephrine & NE is increased.

يعني ال cocaine هتكون عنده كمية ال NE ال ال في ال synaptic cleft
 يبقى لو اديته كمية قليلة من ال catecholamines
 ال effect هياك ← vasoconstriction ← يبقى ال anesthetic
 هينقى في ال nerve ده

Reserpine → prevent uptake of NE into storage vesicles

Guaridine → prevent release of NE into synaptic cleft

Cocaine → prevent reuptake of NE into neurons

يبنى نجمعهم كنه ٥٥٥٥

الدواء الك ٥٥٥

- 1- prevent uptake of NE into storage vesicles
٥٥ Reserpine
- 2- prevent release of NE into synaptic cleft.
٥٥ Guanethidine
- 3- Prevent reuptake of NE into neuron
٥٥ Cocaine

بس كنه ٥٥٥

خلفنا المحاضرة وخلصنا ال autonomus ك

*المرة الجاية د/ ابتهاج انشاء الله هتكل معنا ال Cardiovascular
الى ابتدياته في المحاضرة الخامسة.

حاولوا تحضروا المحاضرة على ما الدكتور دي شرحها
طو اوى وبتفهم طو ٥٥٥ هتستفيدوا لو جهزتها ٥٥٥

PLZ ٥٥٥ Pray 4 us a lot ٥٥٥

محتاجين فعلاً ملوا تكم اوى ٥٥٥

Urs. Dr/P.S.

*Dr/K.A